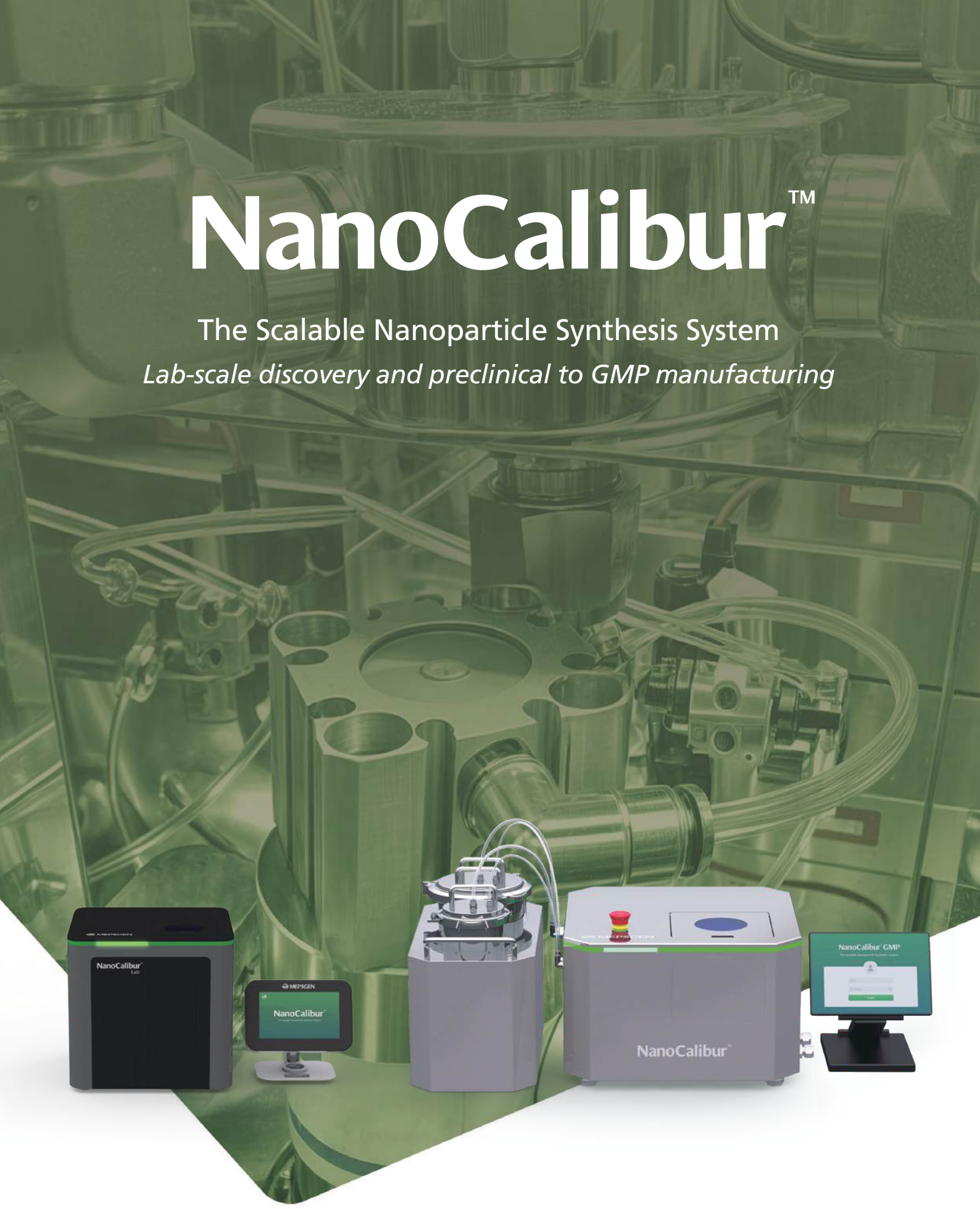
NanoCalibur™

The Scalable Nanoparticle Synthesis System

Lab-scale discovery and preclinical to GMP manufacturing



MEPSGEN

NanoCalibur™ Technologies

NanoCalibur™ provides unprecedented solutions with advanced microfluidic technologies to formulate various types of NPs with precisely defined properties and tunable scalability.

Microvortex mixing patterns engineered to formulate nanoparticles

- These scalable single cartridge units meet a range of throughputs from discovery to preclinical studies with > 95% mixing efficiency for uniform synthesis.

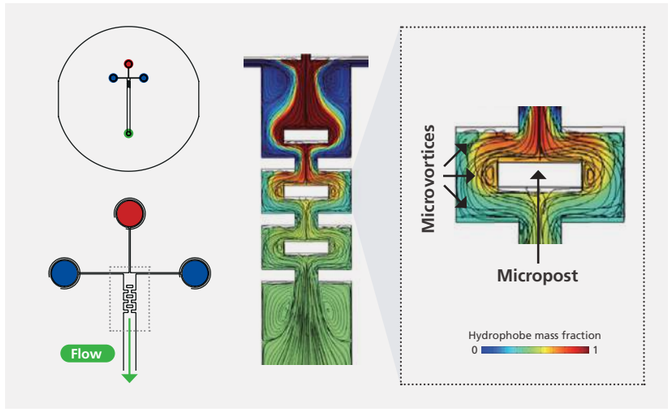
Synthesis chip parallelization for scalable production

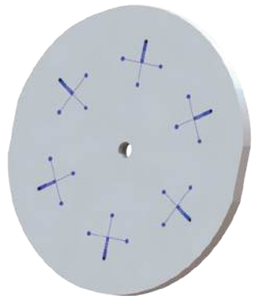
- Microfluidic parallelization preserves the microfluidic pattern of one unit of micromixer and minimizes optimization time in the process of scaling up to mass production with rapid adjustments in production capacity in response to market needs.
- The controlled environment of microfluidic systems reduces variability, leading to more consistent and reproducible outcomes in LNP production and meeting the regulatory compliance for product consistency.
- NanoCalibur™ utilizes a network of MPA126 X1 to distribute the precursor solutions in PMS-cMPA126 and ensure that shear stress remains within critical levels that preserve mRNA integrity.

Dean vortex-induced mixing of MPA126

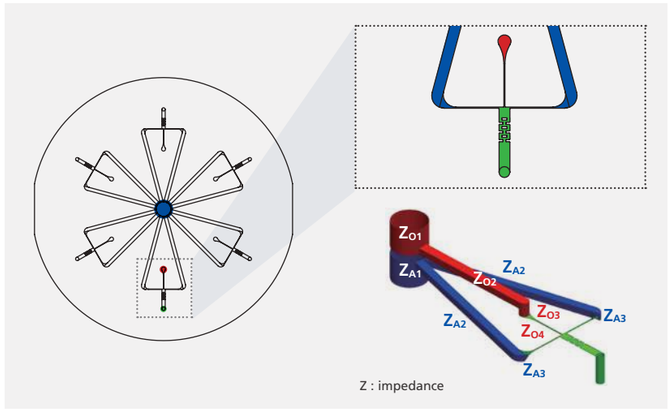
● Organic phase inlet
● Aqueous phase inlet
● Outlet

MPA126 X1
NanoCalibur™ Lab





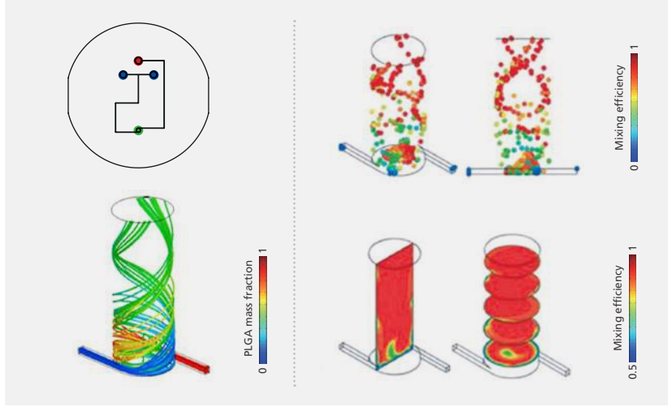
PMS-cMPA126 X16
NanoCalibur™ GMP

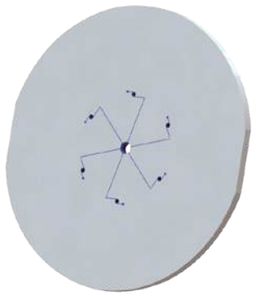


Swirling vortex-induced mixing of SMR25T

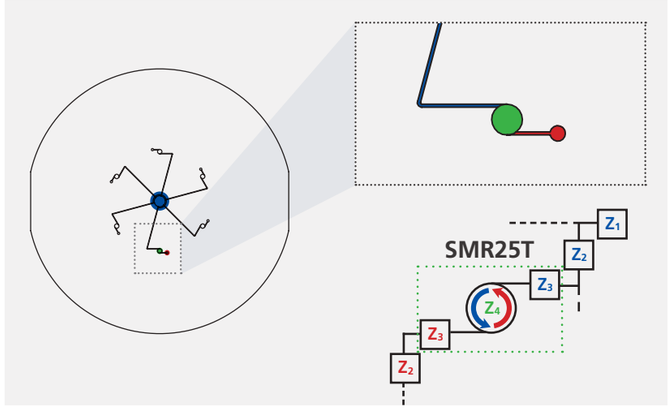
● Organic phase inlet
● Aqueous phase inlet
● Outlet

SMR25 T1
NanoCalibur™ Lab



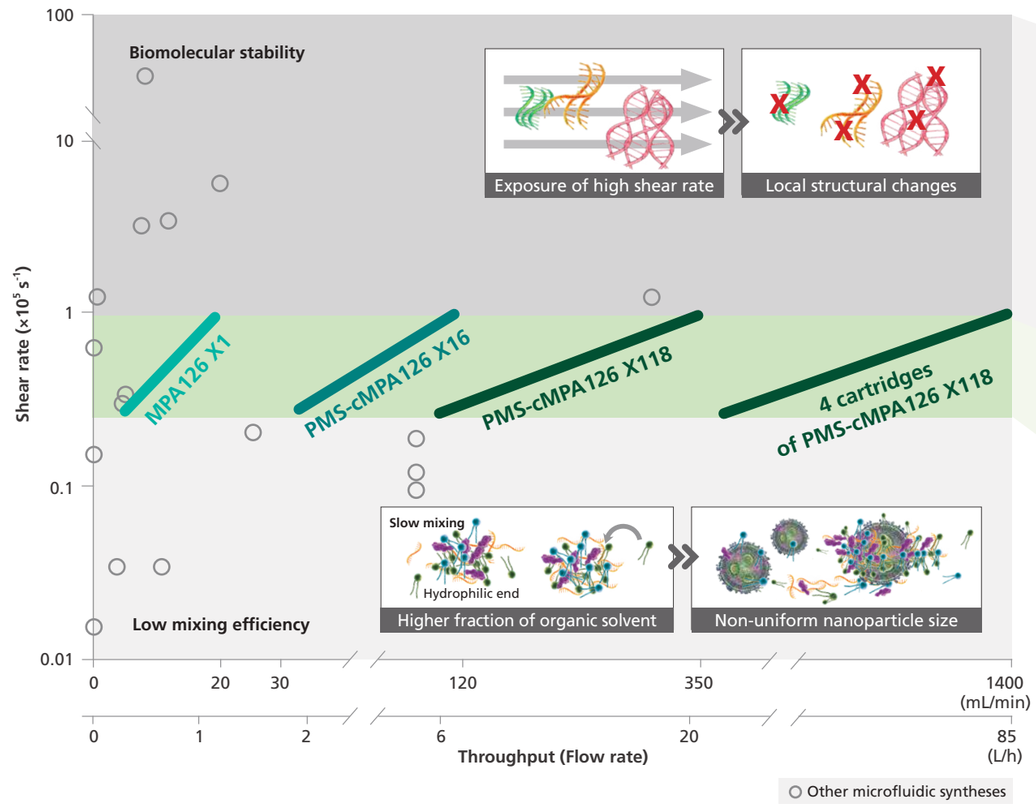


PMS-cSMR25 T16
NanoCalibur™ GMP



Product Line

NanoCalibur™ Lab	NanoCalibur™ GMP	NanoCalibur™ Commercial
		
Small-scale synthesis for discovery and preclinical	GMP level production for preclinical and clinical	GMP to Commercial
2.5 - 20 mL/min (0.15 - 1 L/h)	2 - 6 L/h	6 - 20 up to 80 L/h (with 4 PMS cartridges)



- NanoCalibur™ operates for all the production rates under controlled shear rates at which the produced LNPs are stable and uniform with intact mRNA encapsulated. Other microfluidic syntheses (circle) result in high variability of the size or excessive aggregation of precursors in a lower shear rate, or reportedly cause the decrease in biomolecular stability, possibly leading to loss of therapeutic reagents.

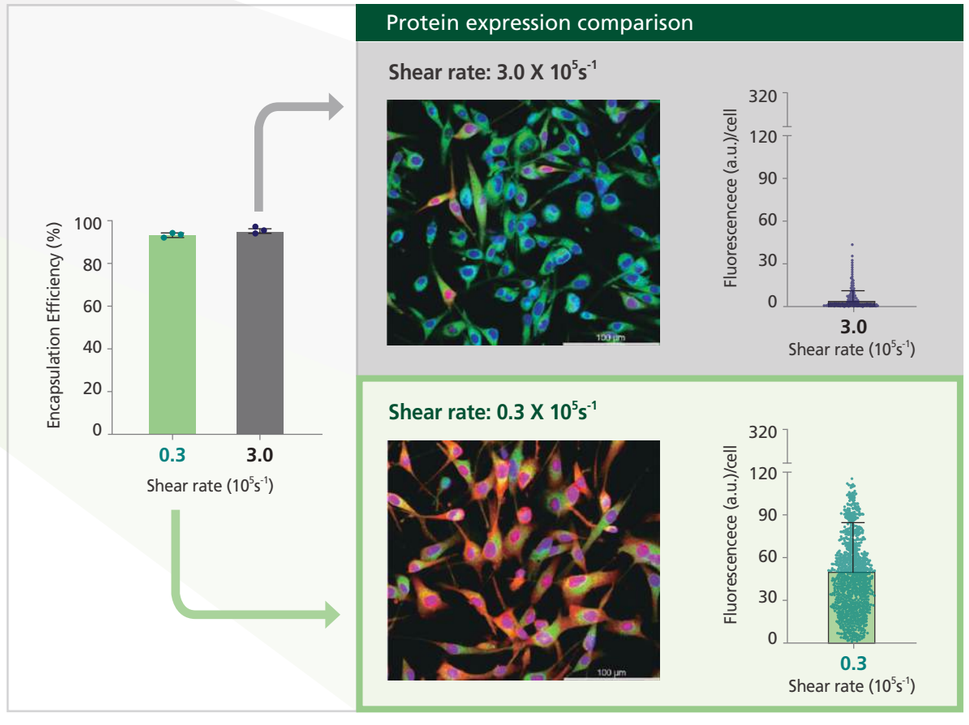
LNP Production Under Controlled Shear Rates Prevents RNA Damages

Microfluidic parallelization minimizes the shear stress exposed to the precursor components

- Shear rates involved in microfluidic mixing at high flow rates reportedly cause the decrease in biomolecular stability, possibly leading to loss of therapeutic reagents such as damaged mRNA.
- NanoCalibur™ distributes the flow of lipid and mRNA solutions across multiple pathways and ensures that shear stress applied to mRNA remains within critical levels that preserve mRNA integrity.

High stability of mRNA under a suitable shear rate mediated mRNA-LNP synthesis

- Cells treated with mCherry LNPs prepared at 0.3 × 10^5 s^{-1} exhibited significantly higher mCherry expression compared to those treated with mCherry LNPs prepared at 3.0 × 10^5 s^{-1}, although the encapsulation efficiency of mRNA-LNPs for both cases of the shear rates remains the same (approximately 95%).
- While shear rates do not significantly alter the physicochemical properties of LNPs and the encapsulation efficiency remains similar under both high and low shear rate conditions, the excessive shear stress during LNP formulation causes mRNA damage and results in significant differences in protein expression.



NanoCalibur™ Lab

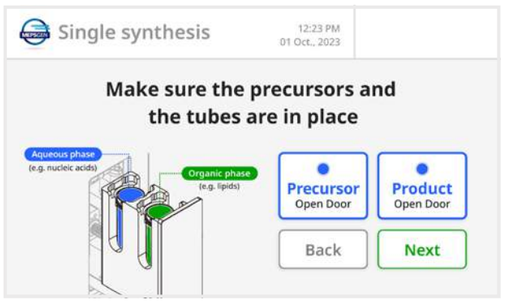
The system offers a user-friendly operation, making lab-scale synthesis and the development of new drug-loaded nanoparticles more accessible. It supports production rates ranging from 2.5 to 20 mL/min (0.15 to 1 L/h).

1 Closed-loop feedback control system and computerized manufacturing

- High-precision flow control by closed-loop pressure regulation for robust manufacturing.
- The continuous feedback loop implemented into the microfluidic synthesis chip facilitates immediate responses to any fluctuations that may affect the produced LNP quality.

2 User-friendly precursor preparation

- Automated operation with no syringe or tubing bundles makes it easier to reliably use for small-scale nanoparticle synthesis.



mRNA : 0.004 ~ 0.3 mg/mL

Lipid : 0.6 ~ 13 mg/mL

6 Product tube multi-holder for multiple syntheses

- Rotatable multi-holder system
- Autonomously designed series of synthesis conditions

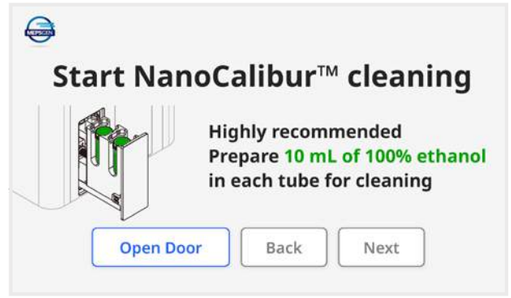
3 Synthesis cartridge made of stainless steel (SUS 316L)

- Semi-permanent use and cost-effective synthesis with no laborious replacement of chips

※ Disposable plastic cartridge available (Optional)

4 Cartridge cleaning protocol

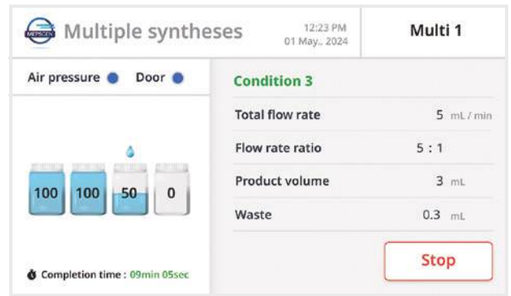
- Cleaning protocols prepared before and after synthesis



5 Touchscreen display

- User-friendly interface for setting the condition and monitoring the progress

※ Optimized conditions indicated in Library:
FRR (Flow Rate Ratio) = 1:5.5
TFR (Total Flow Rate) = 5.2, 10.4, 19.8 mL/min



NanoCalibur™ GMP

A robust nanoparticle production system with integrated synthesis and cleaning processes supports from preclinical animal studies to clinical trials.

1 Precise flow control by integrated mass flow controller (MFC)

- The continuous feedback loop integrated into the microfluidic system ensures that synthesis conditions remain optimal throughout the manufacturing process.
- Enhanced control allows for real-time monitoring and adjustment of flow conditions, facilitating immediate responses to any fluctuations that may affect the product quality.

2 Durable precursor containers for large-scale LNP production

- Maximum pressure of up to 7 bar (101.5 psi) applicable with stainless steel (SUS 316L)

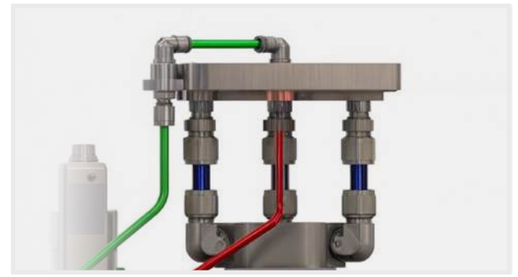
3 Other features of NanoCalibur™ GMP

- Ensuring stable productivity at a liters-per-hour scale through high precision flow control and PMS based synthetic cartridges
- Clean in place (CIP), without relocation or disassembly, to ensure GMP compliance with product quality standards

4 Synthesis cartridge made of stainless steel (SUS 316L)

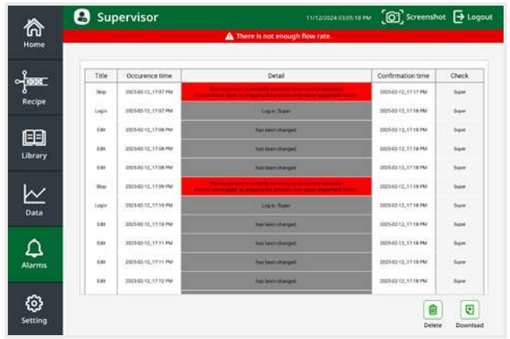
- Semi-permanent use and cost-effective synthesis with no laborious replacement of chips

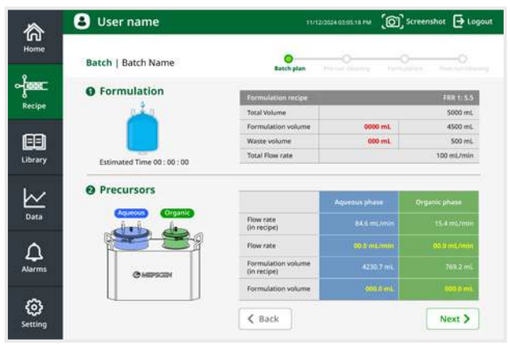
※ Disposable plastic cartridge available (Optional)



5 Logs and user control

- Save all processes as document records
- User-specific administrative records





6 Network

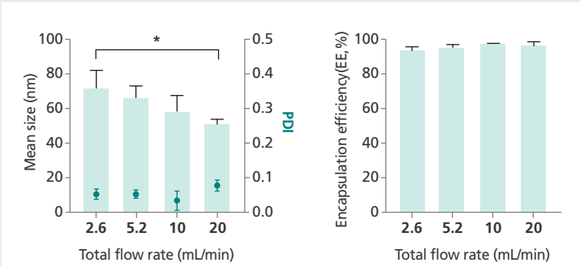
- Built-in Wi-Fi and Ethernet network for seamless data export and firmware upgrades at no additional cost

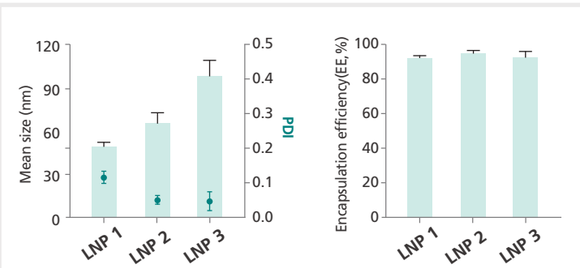
Case Studies

LNP

Uniform and size-controllable production of mRNA-LNPs and ASO-LNPs

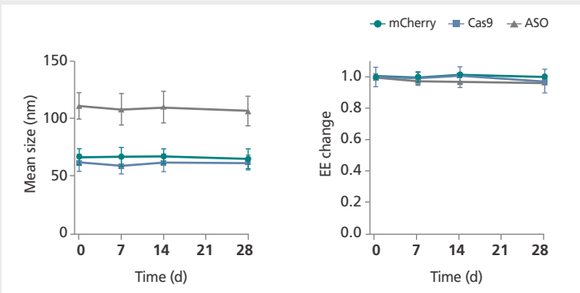
- The size of LNP is varied with the total flow rate under shear rates below 1 × 10^5 s^{-1}, and the payload is encapsulated with > 90% efficiency in all LNPs.
- Uniform LNPs with an encapsulation efficiency of > 90% are produced by MPA126 X1.



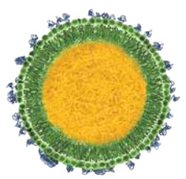


Highly stable payload encapsulation

- Both the size and encapsulation efficiency of LNPs synthesized with a high mixing efficiency of > 95% are maintained for 4 weeks.

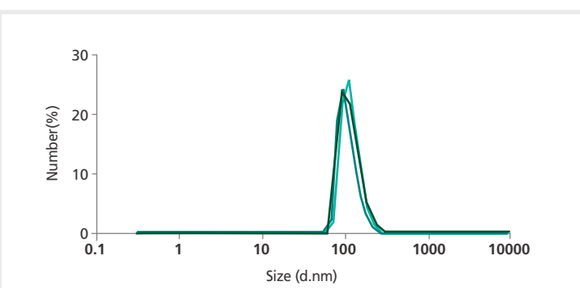


Liposome

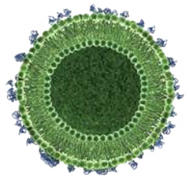


Uniform liposome production

- Liposomes synthesized by MPA126 X1 exhibit a PDI of less than 0.2, demonstrating excellent uniformity.



Lipid-Polymer

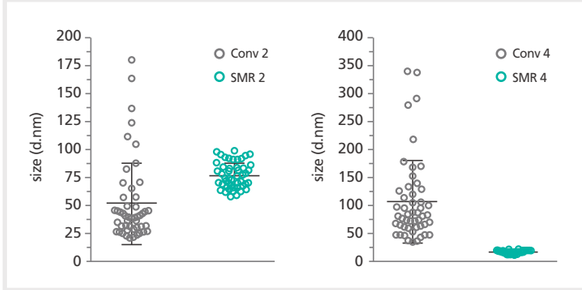


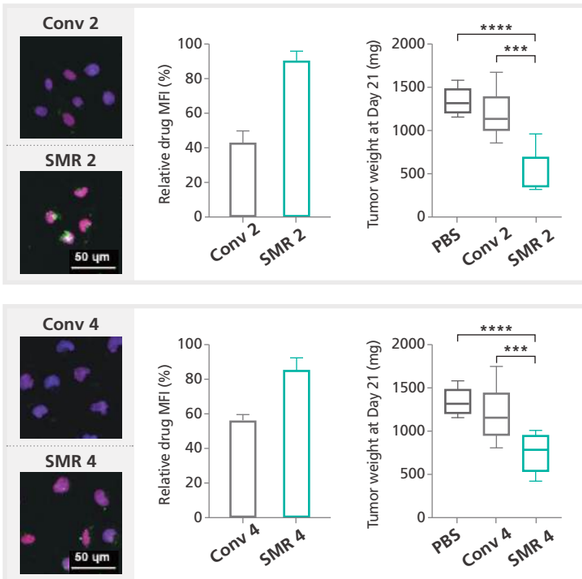
Production of uniformly sized lipid-polymer NPs

- The NPs produced by SMR25 T1 showed a higher size uniformity than the NPs produced by conventional synthesis.

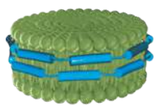
Production of drug-loaded lipid-polymer NPs

- NPs manufacturing technology that enables the production of highly uniform NPs with high drug encapsulation efficiency.
- The NPs produced by SMR25 T1 showed a higher cellular internalization efficiency and anti-tumor effect than the NPs produced by conventional synthesis.
- Efficient NPs mass production through an optimized synthesis system built based on microfluidic technology.



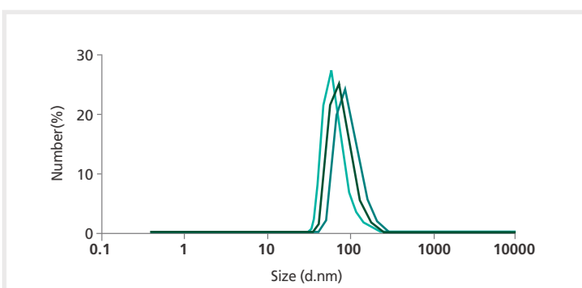


Lipid-Protein



Uniform lipid-protein production

- Both size and uniformity (PDI) of lipid-protein synthesized through high mixing efficiency of MPA126X1 are maintained for 3 months.



[1] Jung, Sungjin, *et al. Advanced healthcare materials* 9.22 (2020): 2001633. **[2]** Toth, Michael J., *et al. Lab on a Chip* 17.16 (2017): 2805-2813. **[3]** Kim, YongTae, *et al. Nano letters* 12.7 (2012): 3587-3591. **[4]** Mieszawska, Aneta J., *et al. Bioconjugate chemistry* 24.9 (2013): 1429-1434.

[5] Sei, Yoshitaka J., *et al. Biomaterials* 170 (2018): 58-69. **[6]** Sanchez-Gaytan, Brenda L., *et al. Bioconjugate chemistry* 26.3 (2015): 443-451. **[7]** Kim, Jinhwan, *et al. Proceedings of the National Academy of Sciences* 117.39 (2020): 24205-24212.

NanoCalibur™ Products

Sales and Service

Sales of the instruments

Sales of the semi-permanent cartridges
(MPA126 X, SMR25 T, and the PMS)

Optimal synthesis conditions of representative NPs provided and updated

Prospective Clients

NanoCalibur™ Lab

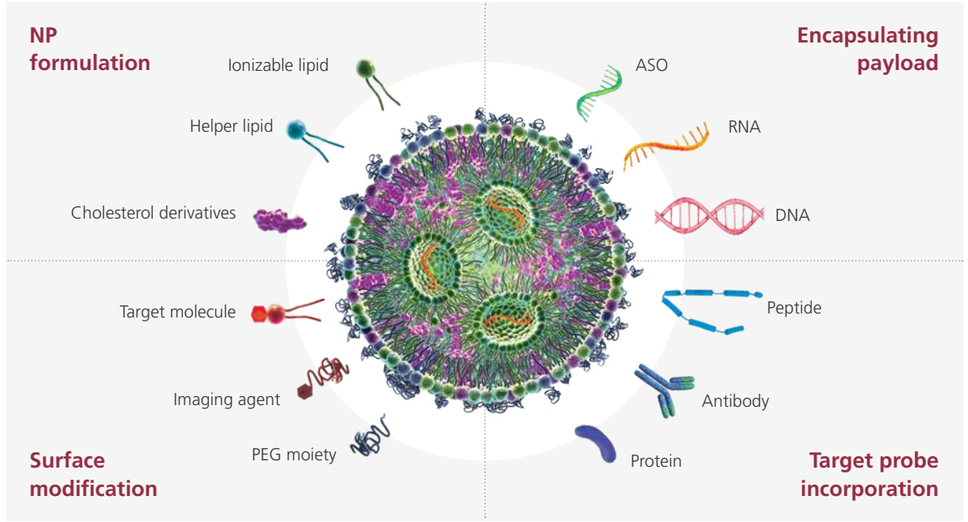
Research laboratories and academic institutions that are developing nanoparticle-based vaccine and therapeutics.

NanoCalibur™ GMP & Commercial

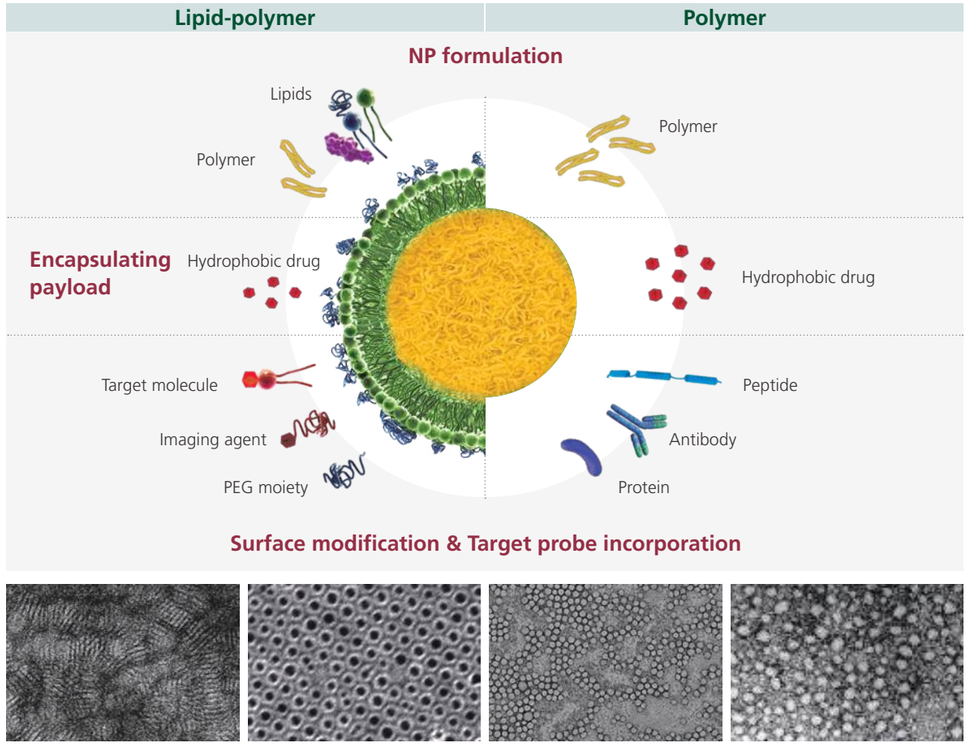
GMP manufacturers that require large-scale production for preclinical studies, clinical trials, and commercial processes.

Nanoparticle Formulation Service

LNP formulation service



Polymeric nanoparticle formulation service



Specifications

NanoCalibur™ Lab

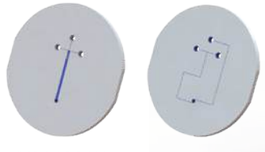
Pressure	Operation pressure		4 bar
	Flow control resolution		0.1 mL/min
Throughput	Total flow rate		2.5 - 20 mL/min
			0.15 - 1 L/h
	Product per run		3 - 90 mL
Container	Precursor container (Conical tube)	Aqueous phase	50 mL
		Organic phase	50 mL
	Product container (Conical tube)	Product & waste	15 mL
General specification	Dimension (W x L x H)		32 cm x 32 cm x 31 cm
	Weight		Total: 27 kg (Instrument: 25 kg, Display: 2 kg)
	Supply voltage		AC 100 V - 240 V
	Power consumption		Max. 230 W
Formulation information of precursors	Total lipid concentration		0.6 - 13 mg/mL
	Nucleic acid concentration		0.004 - 0.3 mg/mL
	Minimum amount of initial mRNA		0.007 mg
Encapsulation efficiency			> 90 %

NanoCalibur™ GMP

Pressure	Operation pressure		Up to 6 bar
	Max. pressure		7 bar
Throughput	Total flow rate		30 - 100 mL/min
			2 - 6 L/h
Container	Precursor container (Stainless steel)	Organic phase	1 L, 2 L
		Aqueous phase	5 L, 10 L
	Precursor housing holder [Dimension (W x L x H)]		24 cm x 46 cm x 30 cm
	Product container (Disposable storage bag)	Product	5 L, 10 L
General specification	Dimension (W x L x H)	Instrument	44 cm x 44 cm x 28 cm
	Weight	Instrument	44 kg
		Precursor housing holder	5 kg
		Precursor containers: Organic (1 L)	4 kg
		Precursor containers: Aqueous (5 L)	9 kg
	Supply voltage		AC 100 V - 240 V, 50/60 Hz
	Power consumption		130 W

Cartridge MPA126 X1, SMR25 T1

General specification	Diameter	100 mm
	Weight	< 1 kg
	Main component	SUS 316L Stainless steel for semi-permanent use



MPA126 X1

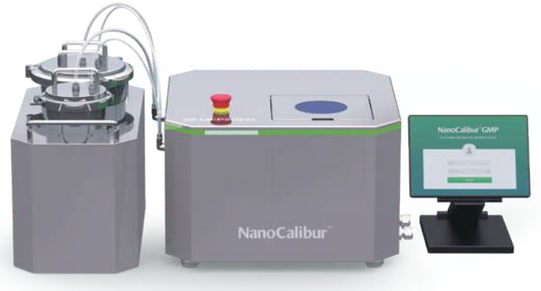
SMR25 T1

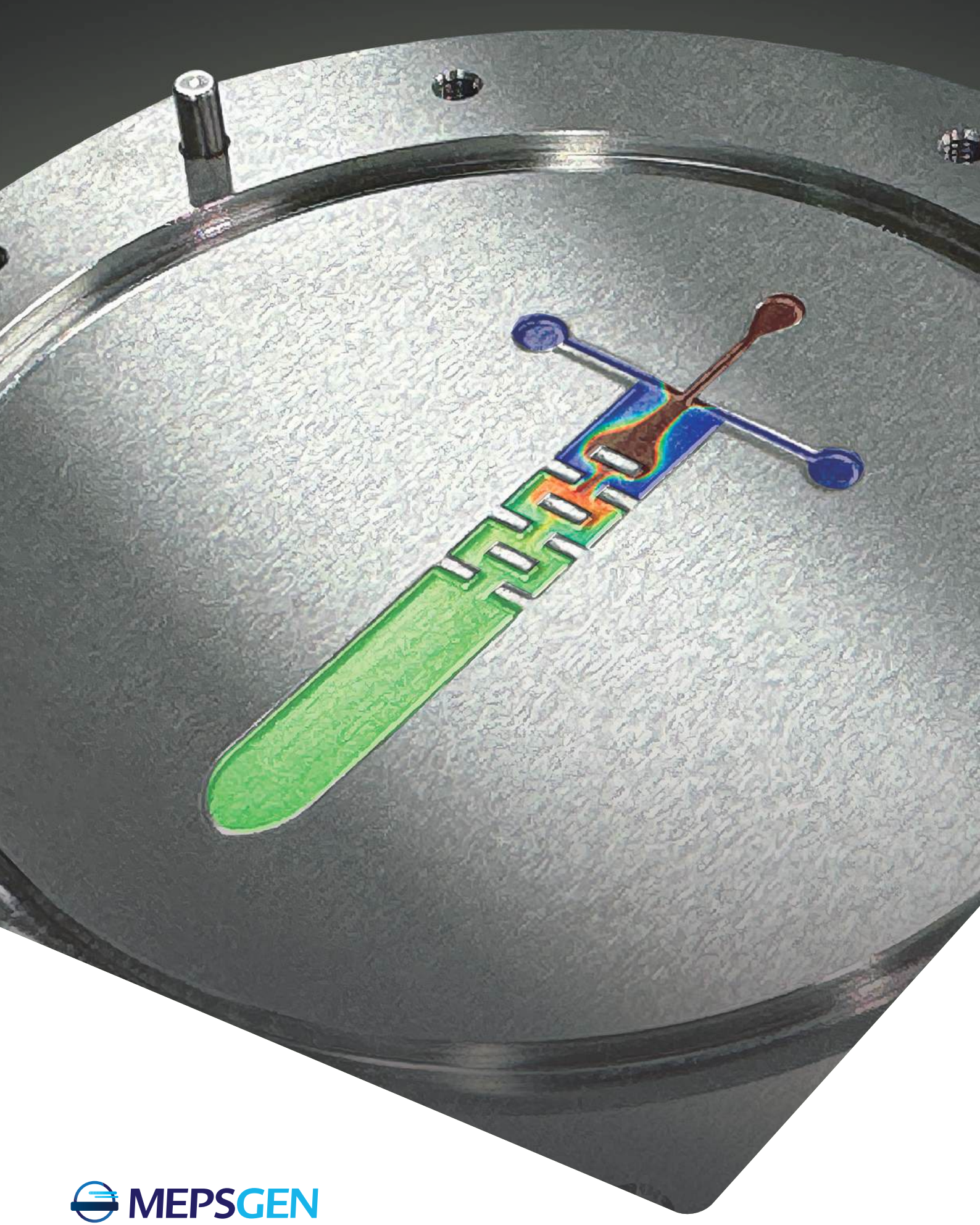
Cartridge PMS-cMPA126 X16, PMS-cSMR25 T16

General specification	Diameter	160 mm
	Weight	< 10 kg
	Main component	SUS 316L Stainless steel for semi-permanent use

PMS-cMPA126 X16

PMS-cSMR25 T16





MEPSGEN

MEPSGEN, 7F, Hanyang Tower, 12, Beobwon-ro-11-gil, Songpa-gu, Seoul, Republic of Korea
Tel +82-2-401-4370 I **Fax** +82-2-400-4855
www.mepsgen.com